



International Journal of Surgery Case Reports

journal homepage: www.casereports.com



A rare cause of arthropathy: An ochronotic patient with black joints



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ARTICLE INFO

Article history:

Received 23 April 2014

Received in revised form 4 June 2014

Accepted 24 June 2014

Available online 27 June 2014

Keywords:

Ochronosis

Alkaptonuria

Joint replacement

Black cartilage

ABSTRACT

INTRODUCTION: Alkaptonuria is an autosomal recessive disorder of metabolism. The pathogenesis of alkaptonuria includes chronic inflammation, degeneration, and eventually osteoarthritis. Ochronotic arthropathy is a rare condition found in patients with alkaptonuria.

PRESENTATION OF CASE: A 60-year-old female presented for evaluation after a 10-year history of low back pain, right hip pain, and bilateral knee pain. A cementless right total hip and a cemented left knee replacement were performed. Intraoperatively, the joint surfaces, neighboring ligaments, and tendons were black with pieces of black cartilage tissue. Histological sections of bone and soft tissue demonstrated classic findings of ochronosis, including multiple pigmented areas, reactive giant cells, and a thickened, inflamed synovium.

DISCUSSION: The management of ochronotic arthropathy in alkaptonuria patients is usually conservative, but replacement surgery is offered for severely affected hip and knee joints. A few reports of the surgical treatment of ochronotic arthropathy have been published. This report describes a case of ochronotic hip and knee arthritis treated with total hip and knee arthroplasties.

CONCLUSION: Joint replacement has excellent outcomes in a patient with significant degenerative arthropathy due to ochronosis.

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1. Introduction

Alkaptonuria is an autosomal recessive disorder of metabolism. It is characterized by homogentisic acid (HGA) deposition in connective tissue as a result of a deficiency in homogentisic acid oxidase, an enzyme involved in the catabolism of tyrosine and phenylalanine.¹ In alkaptonuria, ochronotic pigment is deposited in all connective tissues, especially cartilage. These pigmentary changes are termed ochronosis. Ochronosis can occur in tendons, ligaments, sclera, heart valves, the intima of blood vessels, and the skin.² The irreversible binding of the homopolymeric oxidation products of HGA to collagen causes degenerative changes in the morphologic structure of connective tissue, resulting in fragile complexes. The pathogenesis of alkaptonuria includes chronic inflammation, degeneration, and eventually osteoarthritis. Ochronotic arthropathy is a rare condition found in patients with

alkaptonuria.² The knee is the most common site of joint abnormalities. Other sites of involvement are the hips, shoulders, sacroiliac joints, and lumbar intervertebral discs. There is no specific medical treatment for ochronosis, and generally symptoms are managed as they manifest or worsen. However, in cases of significant degenerative arthropathy, joint replacement can be performed.^{3–5}

2. Case presentation

A 60-year-old female presented for evaluation after a 10-year history of low back pain, right hip pain, and bilateral knee pain. After 4 years, the right hip pain had become constant. At the time of initial evaluation, the patient stated that walking was very painful and limited. She reported that walking up and down stairs was also extremely difficult. She denied any pain at rest or pain at night that interfered with sleep. She had received conservative treatment, which consisted of simple analgesics and physical therapy. Routine laboratory examination of the patient was normal. She had no family history of metabolic abnormalities. One year later, the patient returned to our clinic due to pain and limited hip motion.

Radiographic evaluation of the right hip showed moderately advanced degenerative arthritis, with significant loss of joint space (Fig. 1). A cementless right total hip replacement (PPF; Biomet,

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Fig. 1. Preoperative anteroposterior radiograph of the hips.

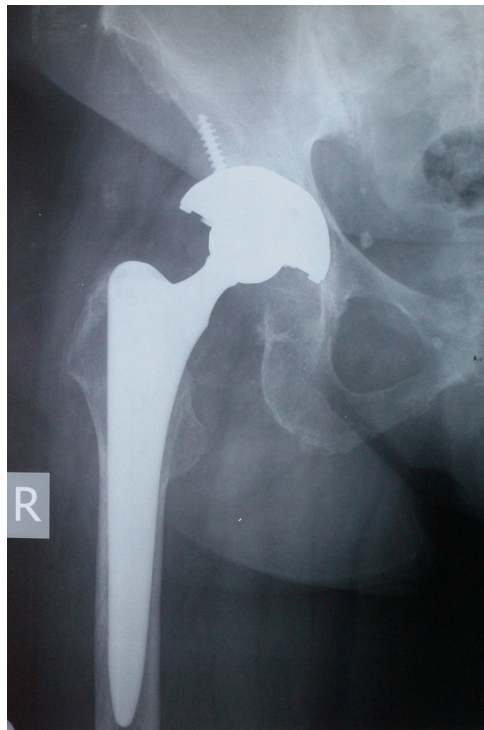


Fig. 2. Postoperative anteroposterior radiograph of the right hip showing cementless total hip prosthesis.

Warsaw, Poland) was performed (Fig. 2). Two years after the hip replacement, the patient was referred to our clinic again due to left knee pain and limitation of motion. During physical examination, she walked with a secure, stable gait that had an antalgic component. Further examination revealed a moderate effusion, with tenderness over the medial and lateral joint line. Mild tenderness was noted on compression of the patella. On range of motion testing, the patient had 10–110° of flexion, accompanied by discomfort in extreme flexion. There was no laxity of the collateral or cruciate ligaments. Radiographic evaluation of the left knee showed moderately advanced degenerative arthritis, with significant loss of medial joint space (Fig. 3a and b). There was more significant involvement of the medial compartment, with less significant lateral and patellofemoral degenerative changes. A cemented total knee arthroplasty (Vanguard; Biomet, Inc., Warsaw, IN) was performed due to progressive pain and stiffness in the patients left knee joint.

Intraoperatively, the joint surfaces, neighboring ligaments, and tendons were black with pieces of black cartilage tissue (Fig. 4a and b). Histological sections of bone and soft tissue demonstrated

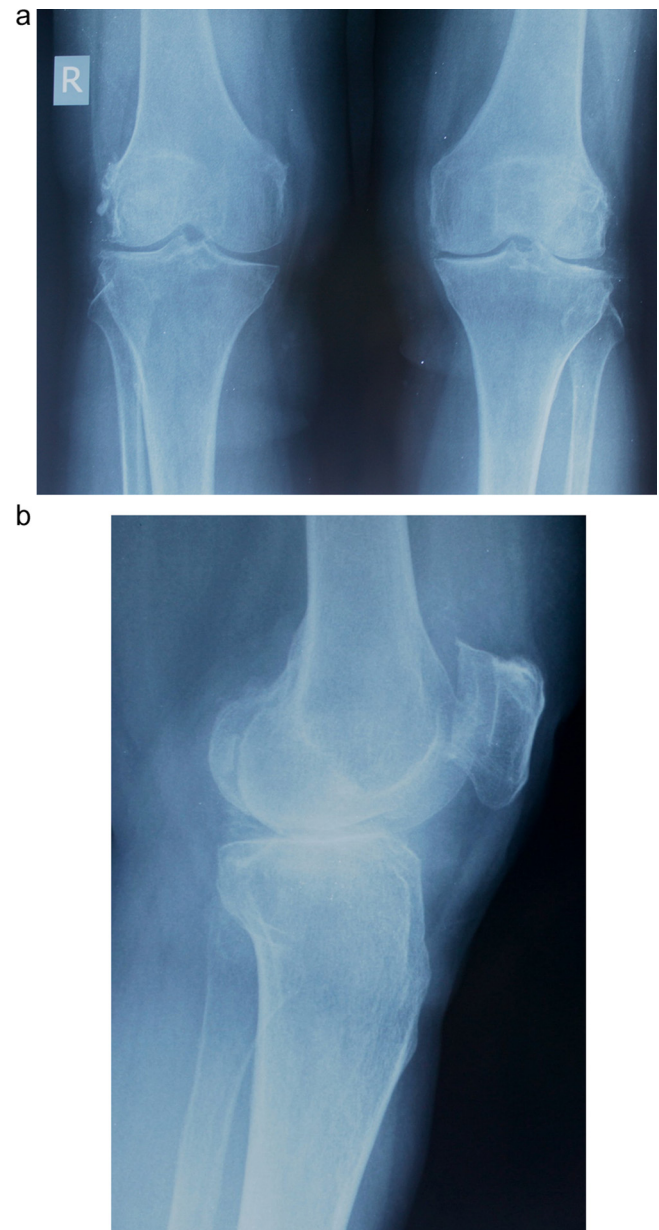


Fig. 3. (a) Preoperative anteroposterior radiograph of the knees. (b) Preoperative lateral radiograph of the left knee.

classic findings of ochronosis, including multiple pigmented areas, reactive giant cells, and a thickened, inflamed synovium. Pathology samples stained with hematoxylin–eosin revealed “synovial stroma, pigmented macrophages, inflammatory cells, and broken glass as material accumulation” at 10× magnification, and at a magnification of 20× “synovial tissues with pigmented cartilage fragments” was observed (Fig. 5a and b).

After the histological diagnosis, the patient was re-examined, but there was no black ochronotic pigmentation of the sclera, cornea, or skin. On examination of the urine, a high level of homogentisic acid was found, and the patient was diagnosed with alkaptonuria.

The patient progressed well postoperatively. During the last follow-up examination, the patient had adequate range of motion and was free of right hip and left knee pain. Plain radiographs did not show any abnormalities in the components of the prostheses (Fig. 6a and b).

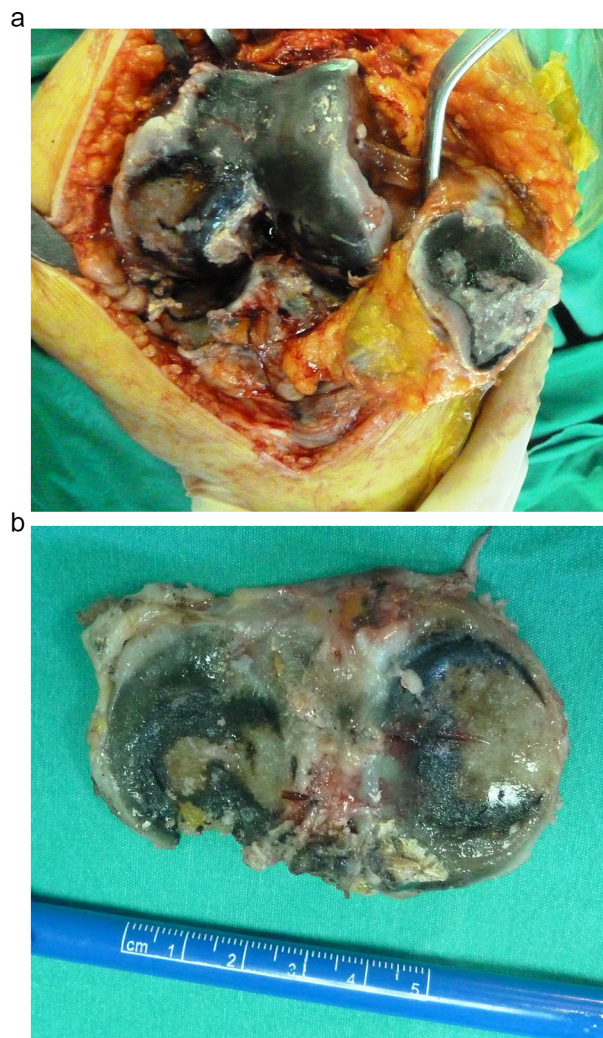


Fig. 4. (a) Intraoperatively the joint surfaces of the ochronotic knee. (b) Intraoperatively resected portion of the tibial plateau.

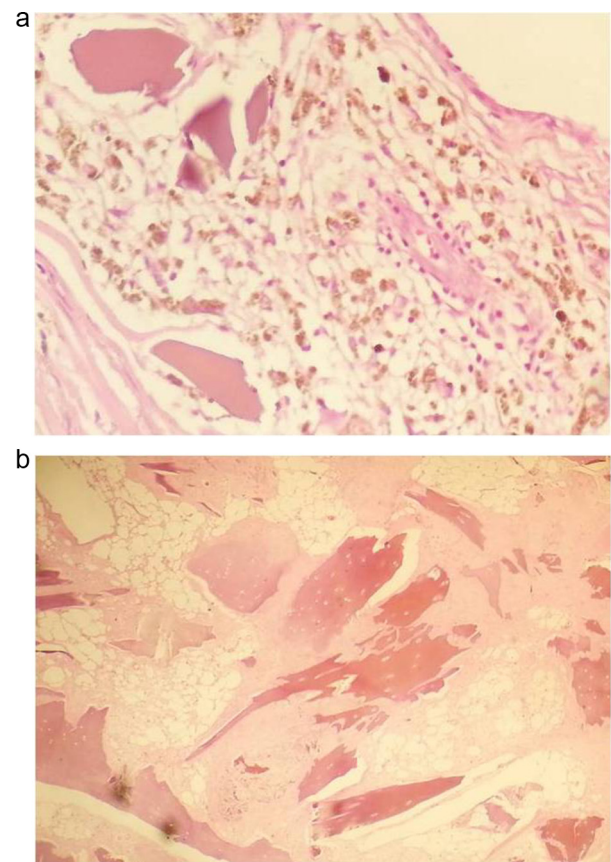


Fig. 5. (a) Microscopic examination revealed “synovial stroma, pigmented macrophages, inflammatory cells, and broken glass as material accumulation” (H&Ex10). (b) Microscopic examination revealed “synovial tissues with pigmented cartilage fragments” (H&Ex20).

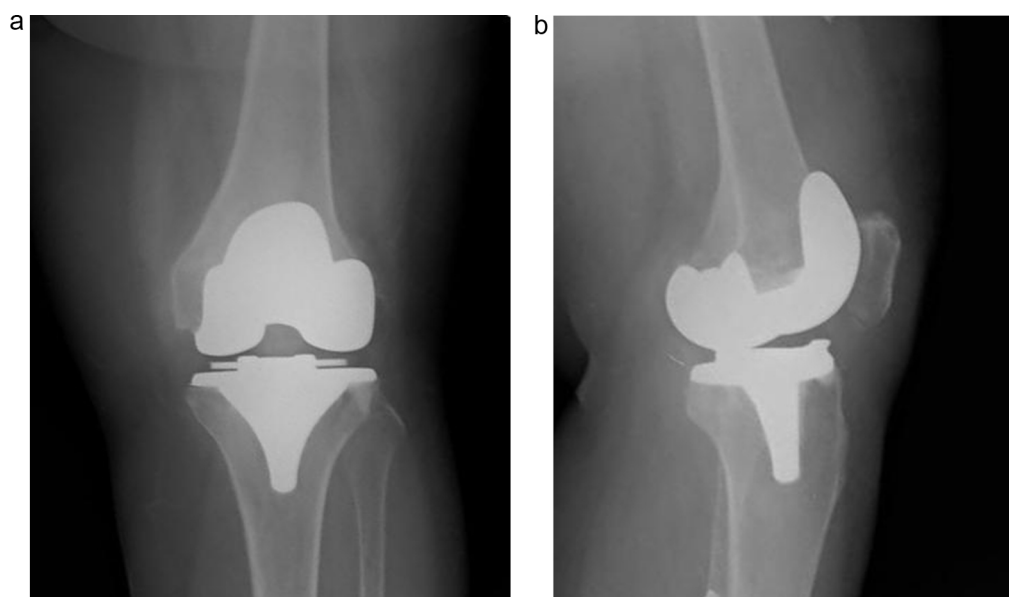


Fig. 6. (a) Postoperative anteroposterior radiograph of the cemented left knee prosthesis. (b) Postoperative lateral radiograph of the cemented left knee prosthesis.

The patient was informed that data concerning her case would be submitted for publication.

3. Discussion

Alkaptonuria is an autosomal recessive metabolic disease that affects one in 250,000–1 million people and is caused by a deficiency in the homogentisic acid oxidase enzyme. This enzyme deficiency causes homogentisate polymers to accumulate and results in urine darkening, brown black pigmentation of connective tissue, articular cartilage pathology, osteoporosis, and pathomorphologic changes in internal organs. The majority of alkaptonuria symptoms are not observed until the fourth decade.^{1,2,6,7} There is no known medical treatment for alkaptonuria.³

The management of ochronotic arthropathy in alkaptonuria patients is usually conservative, but replacement surgery is offered for severely affected hip and knee joints.^{4,8} A few reports of the surgical treatment of ochronotic arthropathy have been published. This report describes a case of ochronotic hip and knee arthritis treated with total hip and knee arthroplasties.

Ochronotic arthropathy is often diagnosed during a total joint replacement and may not be suspected until dark synovium and cartilaginous surfaces are found intraoperatively. In the present case the diagnosis of ochronosis was not made until exploration of the joint. We performed cementless arthroplasty of the hip joint and cemented arthroplasty of the knee joint. The patient received standard physical therapy with satisfactory results.

4. Conclusion

Alkaptonuria patients may be treated supportively, but currently there is no effective medical treatment for ochronosis. Therefore, the orthopedic surgeons should consider alkaptonuria and other metabolic disorders in the differential diagnosis of degenerative disease. Since alkaptonuria is a rare disease, we believe it may be beneficial to pre-screen patients with degenerative disease for signs of ochronosis, as this could aid in the pathologic diagnosis. Joint replacement has excellent outcomes in a patient with significant degenerative arthropathy due to ochronosis.

Conflict of interest

No conflict of interest was declared by the authors.

Funding

The authors declared that this study has received no financial support.

Ethical approval

No ethical approval. This is a retrospective case report.

Author Contributions

HM, HY, SM, CM, FF and UO were involved in the conception, design and interpretation. HY, HM and SM wrote the manuscript. FF, UO, CM and HM collected data, reviewed relevant published reports and provided the images. HM, HY, SM, CM, FF and UO drafted the article or revised it critically for important intellectual content. All authors read and approved the final manuscript.

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